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Date Transmitted: August 8, 2005

CV01492K US
Client No.: 4686 File No.: 045551

Message:

Application No. 056,680
Inventors: Kosoglou et al.
Filed: January 25, 2002
Title: COMBINATIONS OF STEROL ABSORPTION INHIBITOR(S) WITH BLOOD MODIFIERS FOR TREATING VASCULAR INDICATIONS

Transmittal Form (1p)
Response (1p.)
Substitute Brief (18)

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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission	21

Application Number	10/056,680
Filing Date	January 25, 2002
First Named Inventor	T. Kosoglou et al.
Art Unit	1617
Examiner Name	San-Ming R. Hui
Attorney Docket Number	CV01492K – 4686-045551

ENCLOSURES *(check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment / Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts Under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to convert to a Provisional Application
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  - ☐ Landscape Table on CD
- ☐ After Allowance communication to TC
- ☒ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ Other Enclosure(s) (please identify below):

Remarks

Also enclosed

Response (1 pg.)

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

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Signature			
Printed Name	Ann M. Carmoni		
Date	August 8, 2005	Reg. No.	35,972

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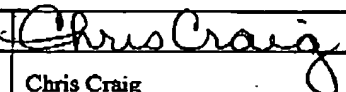
Signature			
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Response Under 37 C.F.R. § 41.37
Appellant's Brief
Application No. 10/056,680
Paper Dated: August 8, 2005
In Reply to USPTO Correspondence of August 2, 2005
Attorney Docket No. CV01492K – 4686-045551

N THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of: T. Kosoglou et al.	Examiner: San-Ming R. Hui
Serial No.: 10/056,680	Group Art Unit: 1617
Filed: January 25, 2002	Atty. Docket No.: CV01492K
For: Combinations of Sterol Absorption Inhibitor(s) with Blood Modifiers for Treating Vascular Indications	

Mail Stop Appeal Brief - Patents
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RESPONSE

Sir:

In response to the Notification of Non-compliant Appeal Brief dated August 2, 2005, Appellant submits the accompanying Substitute Appeal Brief. The Substitute Appeal Brief corrects the informalities set forth in the Notification.

No fee is believed to be due at this time for the filing of the Substitute Appellant's Brief Under 37 C.F.R. § 1.192 as it is being submitted within the allowed thirty (30) day response time. Nevertheless, the Commissioner for Patents is hereby authorized to charge any additional fees which may be required to Deposit Account No. 23-0650.

Respectfully submitted,
THE WEBB LAW FIRM

By _____
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Response Under 37 C.F.R. §1.192
Appellant's Brief

Application No. 10/056,680
Paper Dated: August 8, 2005
Attorney Docket No. CV01492K

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of:
T. Kosoglou et al.

Serial No.: 10/056,680

Filed: January 25, 2002

For: Combinations of Sterol Absorption Inhibitor(s) with Blood Modifiers for Treating Vascular Indications

Examiner: San-Ming R. Hui

Group Art Unit: 1617

Atty. Docket No.: CV01492K

MAIL STOP APPEAL BRIEF – PATENTS
Commissioner for Patents
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Alexandria, VA 22313-1450

ON APPEAL FROM THE PRIMARY EXAMINER TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

SUBSTITUTE APPELLANT'S BRIEF UNDER 37 C.F.R. § 1.192

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08/08/2005 Chris Craig
Date Signature

Chris Craig
Typed Name of Person Signing Certificate

Response Under 37 C.F.R. §1.192
Appellant's Brief

Application No. 10/056,680
Paper Dated: August 8, 2005
Attorney Docket No. CV01492K

TABLE OF CONTENTS

I

REAL PARTY IN INTEREST

The real party in interest in this Appeal is assignee Schering Corporation, having a principal place of business 2000 Galloping Hill Road, Kenilworth, NJ 07033.

II

RELATED APPEALS AND INTERFERENCES

As the legal representative of Appellant, the undersigned attorney has no knowledge of any appeals or interferences directly related to this Appeal.

III

STATUS OF CLAIMS

This is an original patent application in which claims 1 and 3-48 are pending and claims 4-10, 12-17, 21-34, 38-41, 46 and 48 have been withdrawn from consideration by the Examiner. Claim 2 was canceled in the Amendment of May 10, 2004 ("Amendment").

Claims 1-3, 11, 18-20, 35-37, 42-45 and 47 (pending) were finally rejected under 35 U.S.C. § 103(a) in an Office Action mailed July 28, 2004 ("Final Office Action"). Fourteen (14) pending claims (1, 3, 11, 18-20, 35-37, 42-45 and 47) are at issue in this Appeal.

IV

STATUS OF AMENDMENTS

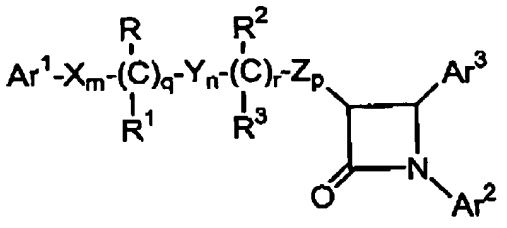
No claims were amended after final rejection. A copy of the claims involved in this Appeal is contained in the Appendix attached hereto.

V

SUMMARY OF CLAIMED SUBJECT MATTER

In embodiments set forth in claims 1 and 47, Applicants have discovered compositions and combinations comprising:

(a) at least one sterol absorption inhibitor represented by Formula (I):



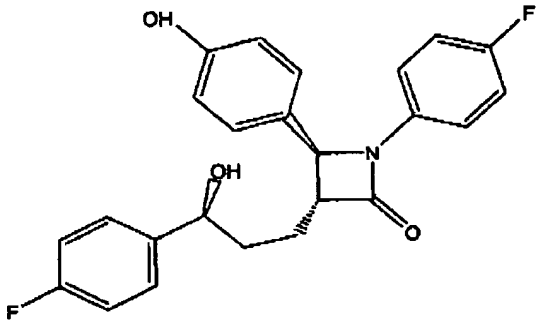
(I)

isomers, prodrugs, or pharmaceutically acceptable salts or solvates thereof (see original claim 2 for moiety definitions); and

(b) at least one blood modifier for vascular conditions which is different from component (a) above

(original claim 2 and page 15, line 23 - page 17, line 4 of the specification).

In the Office Action of August 27, 2003, Applicants were required to elect a species of sterol absorption inhibitor, blood modifier, and third therapeutic agent. Applicants provisionally elected ezetimibe, which is represented by Formula (II) below:



(II).

Ezetimibe is the active ingredient in ZETIA® pharmaceutical formulation, which is commercially available from MSP (Merck Schering-Plough) Pharmaceuticals, Inc. See Response to Restriction Requirement and Election of Species of September 9, 2003 ("Response").

In the same Response, Applicants provisionally elected aspirin as the blood modifier and simvastatin (an HMG CoA reductase inhibitor) as the third therapeutic agent.

The claimed compositions, combinations and treatment methods can be useful for treating vascular conditions and/or lowering concentration of a sterol in plasma in a mammal (page 72, lines 13-18 of the specification).

VI

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. Has a Prima Facie Case of Obviousness Under 35 U.S.C. § 103 Over EP 0720599 ("Rosenblum et al.") and WO 99/47123 ("Ullah") in view of Frei (Proc Soc Exp Biol Med. 1999 Dec; 222(3): 196-204) been Established?

VII

ARGUMENT

II. The Required Prima Facie Case of Obviousness of Claims 1-3, 11, 18-20, 35-37, 42-45 and 47 Under 35 U.S.C. § 103 Over EP 0720599 and WO 99/47123 in View of Frei has Failed to be Established

A. The Rejection

Claims 1, 3, 11, 18-20, 35-37, 42-45 and 47 have been rejected under 35 U.S.C. § 103(a) over EP 0720599 ("Rosenblum et al.") and WO 99/47123 ("Ullah") in view of Frei (Proc Soc Exp Biol Med. 1999 Dec; 222(3): 196-204).

The reasons for rejection are set forth in the Final Office Action, summarized as follows:

In the Office Action, it is alleged that Rosenblum et al. disclose that compositions including the compound of Formula II can be combined with HMG CoA reductase inhibitors such as simvastatin to reduce cholesterol and risk of atherosclerosis (Final Office Action at page 3). Ullah teaches a composition comprising statins, such as simvastatin, in combination with aspirin, for cholesterol lowering and treating or reducing the risk of developing atherosclerosis (Final Office Action at page 3).

It is acknowledged that the primary references do not expressly teach the claimed composition comprising the compound of Formula II, aspirin and

simvastatin together or that antioxidants be incorporated into such as composition (Final Office Action at page 3). It is alleged that Frei teaches that antioxidants such as vitamins C or E can be useful for inhibiting atherogenesis and normalizing vascular functions. (Final Office Action at page 4).

It is further alleged that it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the compound of Rosenblum et al. into Ullah, which are known to be useful to reduce cholesterol level and the risk of atherosclerosis individually, into a single composition useful for the very same purpose, citing *In re Kerkoven*, 205 U.S.P.Q. 1069 (Final Office Action at page 4). Further, it is argued that one of ordinary skill in the art would have been motivated to include an antioxidant since vitamin C, an antioxidant, is known to inhibit the development of atherosclerosis (Final Office Action at page 4).

B. The Prior Art

Rosenblum et al. disclose the compound of Formula II (Page 29, Ex. 6). Rosenblum et al. disclose starch-based pharmaceutical compositions including compounds of Formula I of Rosenblum et al. (Ex. A and B Page 29). Rosenblum et al. teach that the active compounds therein can be combined with HMG CoA reductase inhibitors, such as simvastatin (Page 5, paragraph 0028). Rosenblum et al. also disclose that the active compounds are useful for reducing cholesterol and the risk of atherosclerosis (claims).

Ullah discloses the use of aspirin for reducing myocardial infarction and a statin (such as simvastatin) for lowering cholesterol and preventing or treating atherosclerosis at page 1, lines 14-18, in combination.

Frei discloses that antioxidants may inhibit atherogenesis and improve vascular function by two different mechanisms (Abstract). Lipid-soluble antioxidants present in LDL, such as vitamin C, can inhibit LDL oxidation (Abstract). Antioxidants present in the cells of the vascular wall decrease cellular production and release of reactive oxygen species (ROS), inhibit endothelial activation and improve the biologic activity of ENDO (Abstract).

C. The Required Prima Facie Case of Obviousness Under 35 U.S.C. § 103 Has Not Been Established

When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a prima facie case of obviousness. In re Fritch, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). The Examiner can satisfy this burden only by showing an objective teaching in the prior art, or knowledge generally available to one of ordinary skill in the art, which would lead an individual to combine the relevant teachings of the references [and/or the knowledge] in the manner suggested by the Examiner. Id.; In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

The mere fact that the prior art could be modified does not make the modification obvious *unless the prior art suggests the desirability of the modification* (emphasis added). In re Fritch, 23 U.S.P.Q.2d at 1784; In re Laskowski, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989); In re Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984).

"The ultimate determination of patentability must be based on consideration of the entire record, by a preponderance of evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence." Manual of Patent Examining Procedure, (Rev. 1, Feb. 2003) § 716.01(d) and In re Oetiker, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992).

Claims 1, 3, 11, 18-20 and 47

Claims 1 and 47 recite a composition and therapeutic combination, respectively, comprising a sterol absorption inhibitor of Formula I shown above, isomers, prodrugs, or pharmaceutically acceptable salts or solvates thereof; and at least one blood modifier for vascular conditions which is different from the sterol absorption inhibitor.

Claim 3 depends from claim 1 and recites the compound of Formula II (ezetimibe) as the compound of Formula I.

Claim 11 depends from claim 1 and recites specific groups of blood modifiers. Claims 18-20 depend directly or indirectly from claim 1 and recite that the blood modifier is a platelet inhibitor, such as aspirin.

It is respectfully submitted that the combination of the references cited as rendering the claimed invention obvious is improper because there is no suggestion in the cited references to combine the claimed components of sterol absorption inhibitor (such as that of Formula (I) (e.g., ezetimibe)) and blood modifier such as aspirin.

Applicants wish to emphasize that claim 1 does not require the presence of a third component, such as a statin.

With respect to patentability of a composition or combination of a sterol absorption inhibitor and blood modifier such as aspirin (*without the presence of a statin*), Rosenblum does not suggest or disclose combinations of a sterol absorption inhibitor and blood modifier such as aspirin. Ullah does not suggest or disclose combinations of a sterol absorption inhibitor and blood modifier such as aspirin.

In Ullah, *aspirin is disclosed as being useful for reducing myocardial infarction* at page 1, lines 14-18, *not for treating atherosclerosis*. The statin in Ullah is disclosed as lowering cholesterol and treating atherosclerosis. Id.

In the final Office Action at pages 4 and 5, *In re Kerkoven* was cited as supporting the argument that combining the compositions of Rosenblum and Ullah, which are known to be useful to reduce cholesterol level and the risk of atherosclerosis individually, into a single composition useful for the very same purpose would be considered obvious.

However, the invention of claims 1, 3, 11, 18-20 and 47 is for a sterol absorption inhibitor and blood modifier such as aspirin and does not require a statin. Ullah does *not* disclose aspirin as being useful for lowering cholesterol or treating atherosclerosis. Therefore *In re Kerkoven* does not apply since Ullah does not disclose aspirin as having the same purpose as a cholesterol absorption inhibitor or HMG CoA reductase inhibitor, namely to lower cholesterol or treat atherosclerosis.

Frei does not disclose sterol absorption inhibitors or blood modifiers such as aspirin. Even if the teachings of Frei were combined with those of Rosenblum et al. and Ullah as suggested in the Final Office Action, one skilled in the art would not be motivated to provide a composition having a sterol absorption inhibitor and blood modifier such as aspirin.

Therefore, the prima facie case of obviousness based upon Rosenblum et al., Ullah and Frei has not been established and the rejection of claims 1, 3, 11, 18-20 and 47 should be reconsidered and withdrawn.

Claims 35-37

Claims 35-37 depend from claim 1 and further recite at least one HMG CoA reductase inhibitor, such as simvastatin. Thus the composition would comprise sterol absorption inhibitor, blood modifier such as aspirin, and HMG CoA reductase inhibitor, such as simvastatin.

It is respectfully submitted that the combination of the references cited as rendering the claimed invention obvious is improper because there is no suggestion in the cited references to combine the claimed components of sterol absorption inhibitor (such as that of Formula (I) (e.g., ezetimibe)), blood modifier such as aspirin, and HMG CoA reductase inhibitor.

Rosenblum et al. and Ullah provide no motivation for a triple combination of sterol absorption inhibitor, blood modifier such as aspirin, and HMG CoA reductase inhibitor. Frei only discloses antioxidants as useful for treating atherosclerosis and therefore is not relevant to the rejection of these claims.

Therefore, the prima facie case of obviousness based upon Rosenblum et al., Ullah and Frei has not been established and the rejection of claims 35-37 should be reconsidered and withdrawn.

Claims 42-45

Claims 42-45 depend from claim 1 and further recite at least one antioxidant or vitamin. Thus the composition would comprise sterol absorption inhibitor, blood modifier such as aspirin, and antioxidant or vitamin.

Applicants wish to emphasize that claim 1 does not require the presence of a third component, such as a statin.

With respect to patentability of a composition or combination of a sterol absorption inhibitor, blood modifier such as aspirin and antioxidant or vitamin (*without the presence of a statin*), Rosenblum does not suggest or disclose combinations of a sterol absorption inhibitor and blood modifier such as aspirin. Ullah does not suggest or disclose combinations of a sterol absorption inhibitor and blood modifier such as aspirin.

In Ullah, *aspirin is disclosed as being useful for reducing myocardial infarction* at page 1, lines 14-18, *not for treating atherosclerosis*. The statin in Ullah is disclosed as lowering cholesterol and treating atherosclerosis. Id.

In the final Office Action at pages 4 and 5, *In re Kerkoven* was cited as supporting the argument that combining the compositions of Rosenblum and Ullah, which are known to be useful to reduce cholesterol level and the risk of atherosclerosis individually, into a single composition useful for the very same purpose would be considered obvious.

However, the invention of claims 42-45 is for a sterol absorption inhibitor, blood modifier such as aspirin and antioxidant or vitamin. Ullah does *not* disclose aspirin as being useful for lowering cholesterol or treating atherosclerosis. Therefore *In re Kerkoven* does not apply since Ullah does not disclose aspirin as having the same purpose as a cholesterol absorption inhibitor.

Frei does not disclose sterol absorption inhibitors or blood modifiers such as aspirin. Even if the teachings of Frei were combined with those of Rosenblum et al. and Ullah as suggested in the Final Office Action, one skilled in the art would not be motivated to provide a composition having a

having a sterol absorption inhibitor, blood modifier such as aspirin and vitamin or antioxidant.

Therefore, the prima facie case of obviousness based upon Rosenblum et al., Ullah and Frei has not been established and the rejection of claims 42-45 should be reconsidered and withdrawn.

Accordingly, Applicants respectfully request that the § 103(a) rejection of claims 1, 3, 11, 18-20, 35-37, 42-45 and 47 be reconsidered and withdrawn.

Respectfully submitted,

Date: August 8, 2005

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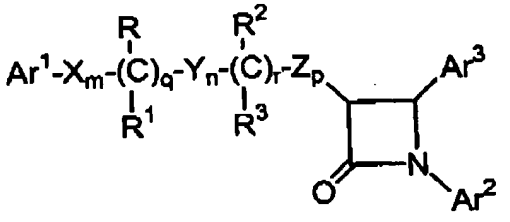
CLAIMS APPENDIX

1. A composition comprising:

(a) at least one sterol absorption inhibitor or pharmaceutically acceptable salt or solvate thereof or prodrug of the at least one sterol absorption inhibitor or of the salt or solvate thereof

wherein the at least one sterol absorption inhibitor is represented by Formula (I):



(I)

or isomers thereof, or pharmaceutically acceptable salts or solvates of the compounds of Formula (I) or of the isomers thereof, or prodrugs of the compounds of Formula (I) or of the isomers, salts or solvates thereof,

wherein:

Ar^1 and Ar^2 are independently selected from the group consisting of aryl and R^4-substituted aryl;

Ar^3 is aryl or R^5-substituted aryl;

X, Y and Z are independently selected from the group consisting of $-CH_2-$, -CH(lower alkyl)- and -C(dilower alkyl)-;

R and R^2 are independently selected from the group consisting of -OR^6,

-$O(CO)R^6$, -$O(CO)OR^9$ and -$O(CO)NR^6R^7$;

R^1 and R^3 are independently selected from the group consisting of hydrogen, lower alkyl and aryl;

q is 0 or 1;

r is 0 or 1;

m, n and p are independently selected from 0, 1, 2, 3 or 4; provided that at least one of q and r is 1, and the sum of m, n, p, q and r is 1, 2, 3, 4, 5

or 6; and provided that when p is 0 and r is 1, the sum of m, q and n is 1, 2, 3, 4 or 5;

R^4 is 1-5 substituents independently selected from the group consisting of lower alkyl, $-OR^6$, $-O(CO)R^6$, $-O(CO)OR^9$, $-O(CH_2)_{1-5}OR^6$, $-O(CO)NR^6R^7$, $-NR^6R^7$, $-NR^6(CO)R^7$, $-NR^6(CO)OR^9$, $-NR^6(CO)NR^7R^8$, $-NR^6SO_2R^9$, $-COOR^6$, $-CONR^6R^7$, $-COR^6$, $-SO_2NR^6R^7$, $S(O)_{0-2}R^9$, $-O(CH_2)_{1-10}-COOR^6$, $-O(CH_2)_{1-10}CONR^6R^7$, -(lower alkylene)$COOR^6$, $-CH=CH-COOR^6$, $-CF_3$, -CN, $-NO_2$ and halogen;

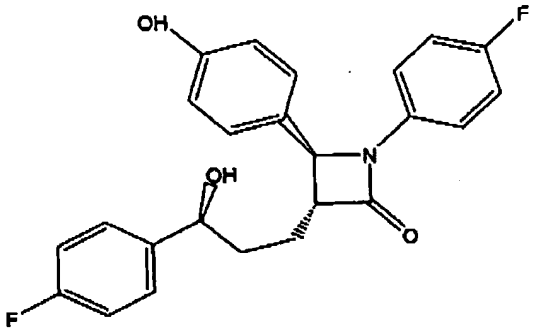
R^5 is 1-5 substituents independently selected from the group consisting of
$-OR^6$, $-O(CO)R^6$, $-O(CO)OR^9$, $-O(CH_2)_{1-5}OR^6$, $-O(CO)NR^6R^7$, $-NR^6R^7$, $-NR^6(CO)R^7$, $-NR^6(CO)OR^9$, $-NR^6(CO)NR^7R^8$, $-NR^6SO_2R^9$, $-COOR^6$, $-CONR^6R^7$,
$-COR^6$, $-SO_2NR^6R^7$, $S(O)_{0-2}R^9$, $-O(CH_2)_{1-10}-COOR^6$, $-O(CH_2)_{1-10}CONR^6R^7$, -(lower alkylene)$COOR^6$ and $-CH=CH-COOR^6$;

R^6, R^7 and R^8 are independently selected from the group consisting of hydrogen, lower alkyl, aryl and aryl-substituted lower alkyl; and

R^9 is lower alkyl, aryl or aryl-substituted lower alkyl; and

(b) at least one blood modifier for vascular conditions which is different from component (a) above.

3. The composition according to claim 1, wherein the sterol absorption inhibitor is represented by Formula (II) below:



(II)

or pharmaceutically acceptable salts or solvates thereof, or prodrugs of the compound of Formula (II) or of the salts or solvates thereof.

11. The composition according to claim 1, wherein the at least one blood modifier is selected from the group consisting of anti-coagulants, antithrombotic agents, fibrinogen receptor antagonists, platelet inhibitors, platelet aggregation inhibitors, hemorrheologic agents, lipoprotein associated coagulation inhibitor, Factor VIIa inhibitors, Factor Xa inhibitors and combinations thereof.

18. The composition according to claim 11, wherein the at least one blood modifier is a platelet inhibitor.

19. The composition according to claim 18, wherein the platelet inhibitor is selected from the group consisting of cilostazol, clopidogrel bisulfate, epoprostenol, epoprostenol sodium, ticlopidine hydrochloride, aspirin, ibuprofen, naproxen, sulindae, idomethacin, mefenamate, droxicam, diclofenac, sulfinpyrazone, piroxicam, dipyridamole and combinations thereof.

20. The composition according to claim 19, wherein the platelet inhibitor is aspirin.

35. The composition according to claim 1, further comprising at least one cholesterol biosynthesis inhibitor.

36. The composition according to claim 35, wherein the at least one cholesterol biosynthesis inhibitor comprises at least one HMG CoA reductase inhibitor.

37. The composition according to claim 36, wherein the at least one HMG CoA reductase inhibitor is simvastatin.

42. The composition according to claim 1, further comprising at least one antioxidant or vitamin.

43. The composition according to claim 1, wherein the at least one blood modifier is administered to a mammal in an amount ranging from about 1 to about 1000 milligrams of blood modifier per day.

44. The composition according to claim 1, wherein the at least one sterol absorption inhibitor is administered to a mammal in an amount ranging from about 0.1 to about 1000 milligrams of sterol absorption inhibitor per day.

45. A pharmaceutical composition for the treatment of vascular conditions, diabetes, obesity or lowering a concentration of a sterol in plasma of a mammal, comprising a therapeutically effective amount of the composition of claim 1 and a pharmaceutically acceptable carrier.

47. A therapeutic combination comprising:

(a) a first amount of at least one sterol absorption inhibitor or pharmaceutically acceptable salt or solvate thereof or prodrug of the at least one sterol absorption inhibitor or of the salt or solvate thereof; and

(b) a second amount of at least one blood modifier different from the sterol absorption inhibitor,

wherein the first amount and the second amount together comprise a therapeutically effective amount for the treatment of vascular conditions, diabetes, obesity or lowering a concentration of a sterol in plasma of a mammal.

EVIDENCE APPENDIX

None.

RELATED PROCEEDINGS APPENDIX

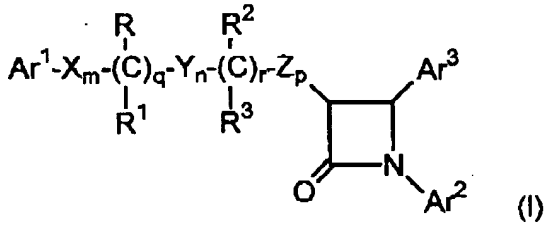
None.

CLAIMS APPENDIX

1. A composition comprising:

(a) at least one sterol absorption inhibitor or pharmaceutically acceptable salt or solvate thereof or prodrug of the at least one sterol absorption inhibitor or of the salt or solvate thereof

wherein the at least one sterol absorption inhibitor is represented by Formula (I):



(I)

or isomers thereof, or pharmaceutically acceptable salts or solvates of the compounds of Formula (I) or of the isomers thereof, or prodrugs of the compounds of Formula (I) or of the isomers, salts or solvates thereof,

wherein:

Ar^1 and Ar^2 are independently selected from the group consisting of aryl and R^4-substituted aryl;

Ar^3 is aryl or R^5-substituted aryl;

X, Y and Z are independently selected from the group consisting of $-CH_2-$, -CH(lower alkyl)- and -C(dilower alkyl)-;

R and R^2 are independently selected from the group consisting of -OR^6,

-$O(CO)R^6$, -$O(CO)OR^9$ and -$O(CO)NR^6R^7$;

R^1 and R^3 are independently selected from the group consisting of hydrogen, lower alkyl and aryl;

q is 0 or 1;

r is 0 or 1;

m, n and p are independently selected from 0, 1, 2, 3 or 4; provided that at least one of q and r is 1, and the sum of m, n, p, q and r is 1, 2, 3, 4, 5